Remarks

Claims 7-12 and 15-18 were pending in the subject application. By this Amendment, the applicants have amended claims 7, 11 and 17, cancelled claim 12 and added new claims 19-22. Support for the claim amendments to claim 7 can be found in the specification as originally filed, at, for example, page 10, lines 6-12; page 13, lines 6-9; page 14, lines 24-27; page 15, lines 3-4 and in Figure 1. Support for the amendment to claim 11 can be found in the specification as originally filed, at, for example, page 10, lines 26-31. Support for new claims 19-21 can be found in the specification as originally filed, at, for example, page 13, lines 6-9; page 14, lines 24-27 and in Figure 1. Support for new claim 22 can be found in the specification as originally filed, at, for example, page 11, lines 5-11.

No new matter has been added by these Amendments. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 7-11 and 15-22 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

The amendments and claim cancellations set forth herein have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 17 and 18 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The applicants respectfully traverse this ground for rejection because the skilled artisan could readily practice the claimed method without the need for undue experimentation.

The applicants respectfully submit that the Office Action characterization of the term "prevent" as requiring absolute cessation is in error because it does not reflect the meaning of that term as it would be understood by one skilled in this art. According to www.wikipedia.org, "in medicine, prevention is any activity which reduces the burden of mortality or morbidity from disease." Prevention can occur "at primary, secondary and tertiary prevention levels." While "primary prevention avoids the development of a disease, secondary and tertiary levels of

prevention encompass activities aimed at preventing the progression of a disease and the emergence of symptoms as well as reducing the negative impact of an already established disease by restoring function and reducing disease-related complications." Accordingly, the applicants respectfully submit that the term "prevent", when afforded its ordinary and customary meaning in this art, does not equate to absolute cessation.

Furthermore, the applicants are submitting herewith an Expert Declaration under 37 CFR §1.132 providing evidence of the ability to prevent disease as set forth in the applicants' claims. This evidence includes experimental results showing the immunopotentiating activity of the high molecular weight phosphorylated dextrans of the subject invention.

It is important to bear in mind that for an invention to be enabled under the first paragraph of §112, the specification need only teach a person of ordinary skill in the art "how to make" and "how to use" the invention.

The requirement for some experimentation and/or screening does not necessarily make a claim non-enabled. "Enablement is not precluded by the necessity for some experimentation such as routine screening. . . A considerable amount of experimentation is permissible, if it is merely routine . . ." (emphasis added). *In re Wands,* 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988).

The applicants are cognizant of the duty under §112, first paragraph, to provide sufficient teaching in the specification to enable one skilled in the art to practice the invention as claimed without undue experimentation. For the reasons set forth above, the applicants believe that they have fulfilled the requirements of 35 USC §112. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Thus, for the reasons given above, the applicants submit that the scope of the claims as amended herein is commensurate with the instant specification's scope of enablement. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph in view of the amendments to the claims and the remarks herein.

Claims 7-9, 17 and 18 have been rejected under 35 U.S.C. §102(e) as being anticipated by King (US patent publication 2004/0224922). The applicants respectfully traverse this ground for

rejection because the cited reference does not disclose the applicants' unique and advantageous methods as claimed herein.

According to the Office Action, the King reference discloses pharmaceutical compositions comprising charged dextran phosphate, said pharmaceutical compositions being able to decrease mucus viscoelasticity and increase mucociliary clearability and therefore useful in the treatment of respiratory disorders such as bronchial asthma (a known "allergic disease"). While King does not explicitly describe the effect of "immunopotentiating" the cell or inducing blastogenesis or interferon, the Office Action deems this to be an inherent effect of the prior art method. As such, the Office Action finds the King reference to anticipate the method of the pending claims.

First, while the King reference proposes the use of dextran phosphate, all the supporting data is directed to dextran sulfate.

The applicant respectfully points out that for a claim to be anticipated under the principles of inherency, the subject of a single prior art reference must necessarily function in accordance with the limitations of the process or method claimed. *In re King*, 801 F2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Further,

> the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation. . . . A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ 2d 1001, 1032-33 (E.D. KY 1988).

One cannot assert with any degree of certainty that dextran phosphate would possess pharmaceutical activity analogous to that of dextran sulfate.

Furthermore, King specifies the use of low molecular weight dextran, preferably dextran dimers ranging from 500 to 5000 daltons (see King, paragraph [0022]). There is no disclosure or suggestion of using high molecular weight dextran, on the order of 100,000, as is required by the applicants' claims.

It is a basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra; Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

The King reference fails to disclose or suggest, explicitly or otherwise, the immunopotentiating ability of a phosphorylated dextran having a molecular weight of at least 100,000 (as required by the claims as amended herein), much less a molecular weight on the order of 500,000 (as specified in new claims 19 and 21). Therefore, the King reference does not anticipate the currently pending claims.

Accordingly, in view of the amendments to the claims and the remarks herein, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) as being anticipated by King.

Claim 11 has been rejected under 35 U.S.C. §102(b) as being anticipated by Suzuki *et al.* 1977 (*Carbohydrate Research* 53(2):223-229). The applicants respectfully traverse this ground for rejection because the cited reference does not disclose each and every element of the claimed method for producing a phosphorylated dextran.

The Office Action indicates that Suzuki *et al.* disclose a phosphorylated dextran and a method of making dextran phosphate that involves reacting dextran with polyphosphoric acid and triethylamine in anhydrous formamide.

In order to lend greater clarity to the claimed subject matter and to expedite prosecution, the applicants have amended claim 11 to clarify that the phosphorylated dextran that is produced by the claimed method has a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the total dextran molecules are phosphorylated. Claim 11 has also been amended to clarify that the step of reacting the dextran with phosphoric acid is done under heat.

As noted above, in order to anticipate a claim, a reference must disclose each and every element of the claim. In this case, Suzuki *et al.* fail to disclose or suggest the reaction of dextran

with phosphoric acid under heat. Furthermore, the Suzuki *et al.* reference fails to disclose or suggest a method for producing an immunopotentiating phosphorylated dextran having a molecular weight of at least 100,000 (as required by the claims as amended herein), much less a molecular weight on the order of 500,000 (as specified in new claim 20), under heat. Therefore, the Suzuki *et al.* reference does not anticipate the invention of the pending claims. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on Suzuki *et al.*

Claims 11 and 12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Japanese Patent Application 52028583 (the '583 application). The applicants respectfully traverse this ground for rejection because the cited reference does not disclose each and every element of the claimed method for producing a phosphorylated dextran.

According to the Office Action, the '583 application discloses a phosphorylated dextran palmitate and a method of making same by heating dextran in a reaction mixture containing various reagents, including polyphosphate, in a formamide solution. To expedite prosecution, the applicants have amended claim 11 to clarify that the phosphorylated dextran that is produced by the claimed method has a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the total dextran molecules are phosphorylated. Claim 11 has also been amended to clarify that the step of reacting the dextran with phosphoric acid is done under heat.

In the '583 application, palmitic chloride is added to the formamide solution that contains dextran and tri-n-butylamine and the mixture is kept at 70° C for two hours (page 459, upper left column, lines 9-15). Then, polyphosphoric acid is added to the mixture, stirred, and the resulting solution is left at room temperature for 24 hours. Accordingly, like Suzuki (Carbohydrate Res), Suzuki (JP 52028583) fails to disclose or suggest the reaction of dextran with phosphoric acid under heat. Moreover, the sole example of the '583 application is directed to low molecular weight dextran (MW of about 40,000).

Thus, in that the '583 application reference fails to disclose or suggest a method for producing an immunopotentiating phosphorylated dextran having a molecular weight of at least 100,000 (as required by the claims as amended herein), much less a molecular weight on the order of 500,000 (as specified in new claim 20), wherein the method comprises the step of reacting a

dextran with polyphosphoric acid under heat, it cannot anticipate the invention of the pending claims. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the '583 application.

Claims 7-10 and 15-18 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Bijlsma *et al.* (US Patent No. 6,686,341 and WO 00/57727). The applicants respectfully traverse this ground for rejection.

According to the Office Action, Bijlsma *et al.* discloses foods and/or supplements comprising compositions containing negatively charged non-digestible polysaccharides, such as dextran, containing negatively charged groups, such as phosphate, useful in preventing the entrance of toxic or allergenic substances through the tight junctions of the intestinal wall and finding utility in the treatment of allergy and allergic reactions. While the Bijlsma *et al.* reference does not teach the specific active ingredient phosphorylated dextran, the Office Action concludes that such would have been obvious from the separate teachings of dextran and phosphate.

As noted above, in order to expedite prosecution, the applicants have amended the claims herein to clarify that the phosphorylated dextran that is produced by the claimed method has a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the total dextran molecules are phosphorylated. Claim 11 has also been amended to clarify that the step of reacting the dextran with phosphoric acid is done under heat.

Bijlsma *et al.* describe nutritional compositions containing only "slightly" negatively charged polysaccharides and in fact expressly teaches away from polysaccharides that contain "too many negatively charged groups" (U.S. Patent No. 6,686,341, columns 5-8; WO Pub., pages 7-12). To that end, the Bijlsma *et al.* polysaccharides preferably contain negatively charged groups "in a quantity of 1 negatively charged group per 10 to 10,000 saccharide units" (U.S. pat., column 2, lines 55-60; WO Pub., page 3, lines 16-20). This is in stark contrast to the applicants' claimed phosphorylated dextrans that possess a phosphorylation level on the order of 90% or higher.

In that the Bijlsma *et al.* reference expressly teaches away from the high degree of phosphorylation required by the instant claims, it can neither anticipate nor render obvious the invention of the pending claims. Therefore, the applicants respectfully request reconsideration and withdrawal of the obviousness rejection under 35 U.S.C. §103, based on Bijlsma *et al.*

Claims 7-11 and 15-16 have been rejected under 35 U.S.C. §102(b) as being anticipated by Suzuki *et al.* 1977 (*Cancer Research* 37:3448-3454). The applicants respectfully traverse this rejection of the claims.

According to the Office Action, Suzuki *et al.* discloses the administration to mice of PDP, DP, and PD, agents known to enhance the antibody response of mice against implanted tumor cells. The Office Action finds that this disclosure inherently meets and therefore anticipates the process of the pending claims.

In order to expedite prosecution, the applicants have amended the claims herein to clarify that the phosphorylated dextran that is produced by the claimed method has a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the total dextran molecules are phosphorylated. Claim 11 has also been amended to clarify that the step of reacting the dextran with phosphoric acid is done under heat.

The Suzuki *et al.* disclosure, like those of King and Suzuki (Carbohydrate Res) discussed above, is limited to low molecular weight dextrans (e.g., 38,000) and cannot be used to phosphorylate dextrans of high molecular weights (e.g., 100,000 or more; see specification, page 10, lines 8-10). Thus, in that the Suzuki reference fails to disclose or suggest an immunopotentiating phosphorylated dextran having a molecular weight of at least 100,000 (as required by the claims as amended herein), much less a molecular weight on the order of 500,000 (as specified in new claim 19), it cannot anticipate the invention of the currently pending claims. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on Suzuki *et al.*

Claims 11 and 12 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Suzuki *et al.* 1977 (*Carbohydrate Research* 53(2):223-229) in view of Sacco *et al.* 1988 (*Carbohydrate Research* 184:193-202). The applicants respectfully traverse this ground for rejection.

According to the Office Action, it would have been obvious to one of ordinary skill in the art to modify the Suzuki *et al.* process to include a heating step in view of the teachings of Sacco *et al.*

To expedite prosecution the applicants have amended the claims herein to clarify that the phosphorylated dextran that is produced by the claimed method has a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the total dextran molecules are phosphorylated. Claim 11 has also been amended to clarify that the step of reacting the dextran with phosphoric acid is done under heat.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See M.P.E.P. §2142, 2143.

In the current case, there is no apparent reason to modify the readings of the cited references to arrive at the current invention. As the CAFC has established, an invention will not be rendered obvious merely by combining teachings found in the prior art. *ACS Hospital Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). There must be some suggestion or incentive in the prior art to make the combination. *Id.* Also, the prior art must suggest that this combination would have a reasonable likelihood of success. *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). The suggestion to make the combination and likely success may not be gleaned from the applicant's disclosure. *Id.*

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.* In this case, the applicants respectfully submit that there is no reason to modify the cited references to arrive at the current invention and, thus, there is no *prima facia* case of obviousness.

Furthermore, the Office Action has summarily dismissed the inclusion of a heating step as "obvious," despite the fact that Examples of the present application conclusively demonstrate the criticality of this step as well as the unexpected superior results arising therefrom.

It is well settled that the presence of a property not possessed by the prior art is evidence of nonobviousness. Herein, by adding a heating step to the prior art methods, the applicants are able to increase the yield by 30%, increase the phosphorylation levels from about 50% to at least 90%, and allow the reaction to be applicable to high molecular weight dextrans (*e.g.*, dextrans of 100,000 daltons or more). These significant yet surprising results are sufficient to establish that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. This provides objective evidence of non-obviousness that is sufficient to rebut any finding of *prima facie* obviousness. Accordingly, the applicants respectfully request reconsideration and withdrawal of the obviousness rejection under 35 U.S.C. §103 based on Suzuki in view of Sacco.

In view of the foregoing remarks and the amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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DRS/la

Attachments: Expert Declaration of Haruki Kitazawa under 37 CFR §1.132; and
Experimental Results